Flame Retardant Alternatives

Proprietary D: Reactive brominated flame retardant

Hazard Review

Proprietary D: Reactive brominated flame retardant
Existing Data Summary Table – Human Health Endpoints

✓= Endpoint characterized by existing data * = Data available but not adequate ✘ = Endpoint not applicable

As noted in this key, a check mark indicates that an endpoint was adequately characterized by existing studies. It does not indicate a positive or negative result for that particular endpoint.

Acute Toxicity	
Oral	*
Dermal	*
Inhalation	*
Eye irritation	*
Dermal irritation	*
Skin sensitization	
Subchronic Toxicity	
28-Day oral	
90-Day oral	
Combined repeated dose with reproduction/ developmental toxicity screen	
21/28-Day dermal	
90-Day dermal	
90-Day inhalation	
Reproductive Toxicity	
Reproduction/ developmental toxicity screen	
Combined repeated dose with reproduction/ developmental toxicity screen	
Reproduction and fertility effects	

Developmental Toxicity	
Reproduction/ developmental toxicity screen	
Combined repeated dose with reproduction/ developmental toxicity screen	
Prenatal developmental	
Chronic Toxicity	
Chronic toxicity (two species)	
Combined chronic toxicity/ carcinogenicity	
Carcinogenicity	
Carcinogenicity (rat and mouse)	
Combined chronic toxicity/ carcinogenicity	

Neurotoxicity	
Acute and 28-day delayed neurotoxicity of organophosphorus substances (hen)	✘
Neurotoxicity screening battery (adult)	
Developmental neurotoxicity	
Additional neurotoxicity studies	
Immunotoxicity	
Immunotoxicity	
Genotoxicity	
Gene mutation in vitro	*
Gene mutation in vivo	
Chromosomal aberrations in vitro	
Chromosomal aberrations in vivo	
DNA damage and repair	

Proprietary D: Reactive brominated flame retardant
Existing Data Summary Table – Properties, Fate, and Ecotoxicity

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As noted in this key, a check mark indicates that an endpoint was adequately characterized by existing studies. It does not indicate a positive or negative result for that particular endpoint.

P/Chem Properties	
Water solubility	
Octanol/water partition coefficient	
Oxidation/reduction	
Melting point	
Boiling point	
Vapor pressure	
Odor	
Oxidation/reduction chemical incompatibility	
Flammability	
Explosivity	
Corrosion characteristics	
pH	
UV/visible absorption	
Viscosity	
Density/relative density/bulk density	
Dissociation constant in water	
Henry's Law constant	

Environmental Fate	
Bioconcentration	
Fish	
Daphnids	
Green algae	
Oysters	
Earthworms	
Metabolism in fish	
Degradation and Transport	
Photolysis, atmosphere	
Photolysis, water	
Photolysis in soil	
Aerobic biodegradation	
Anaerobic biodegradation	
Porous pot test	
Pyrolysis	
Hydrolysis as a function of pH	
Sediment/water biodegradation	
Soil biodegradation w/ product identification	
Indirect photolysis in water	
Sediment/soil adsorption/desorption	

Ecotoxicity	
Aquatic Toxicity	
Fish acute LC50	*
Daphnia acute EC50	
Mysid shrimp acute LC50	
Green algae EC50, NOAEC, LOAEC	
Fish chronic NOAEC, LOAEC	
Daphnia chronic NOAEC, LOAEC	
Mysid shrimp chronic NOAEC, LOAEC	
Terrestrial Organism Toxicity	
Bird LD50 (two species)	
Bird LC50 (two species)	
Bird reproduction	
Earthworm subchronic EC50, LC50, NOAEC, LOAEC	

Chemical Identity

Proprietary D: Reactive brominated flame retardant
Synonyms
CAS
MF
MW
SMILES

Human Health Endpoints

ACUTE TOXICITY

Acute Oral Toxicity (OPPTS Harmonized Guideline 870.1100; OECD Guidelines 425, 420, 423, 401)

Conclusion:

The available acute oral toxicity data were judged inadequate to meet the endpoint.

Basis for Conclusion:

An acute oral study to determine the LD_{50} of Proprietary D was conducted on rats, but was available only as an incomplete robust summary.

As described in an incomplete robust summary, Sprague-Dawley rats (5/sex) were administered a single dose of 10,000 mg/kg of Proprietary D orally in corn oil, and observed for 4 hours and then daily for 14 days. No deaths occurred, and no gross lesions were seen at necropsy. Therefore, the LD50 was >10,000 mg/kg (Ref. 2).

Acute Dermal Toxicity (OPPTS Harmonized Guideline 870.1200; OECD Guideline 402)

Conclusion:

The available acute dermal toxicity data were judged inadequate to meet the endpoint.

***Basis for Conclusion*:**

An acute dermal study was conducted in rabbits, but was available only as an incomplete robust summary.

As described in an incomplete robust summary, New Zealand white rabbits (2/sex) were exposed to a single application of 20,000 mg/kg of Proprietary D applied dermally to intact and abraded skin of the back and flank under an occlusive dressing for 24 hours. The dressings were then removed

and the application sites were washed. There were no animal deaths. Therefore, the dermal LD50 was >20,000 mg/kg. Very slight to slight erythema, edema, and atonia were noted during the 14-day observation period (Ref. 2).

Acute Inhalation Toxicity (OPPTS Harmonized Guideline 870.1300 (OECD Guideline 403)

Conclusion:

The available acute inhalation toxicity data were judged inadequate to meet the endpoint.

Basis for Conclusion:

An acute inhalation study in rats was available only as an incomplete robust summary.

As described in an incomplete robust summary, Charles River CD rats (5/sex) were exposed to 0.008 mg/L of Proprietary D as a saturated vapor for 1 hour. There were no animal deaths and no signs of toxicity during the exposure or the 14-day observation period, and no gross lesions were observed at necropsy. Thus, the LC50 was >0.008 mg/L (Ref. 5).

Acute Eye Irritation (OPPTS Harmonized Guideline 870.2400; OECD Guideline 405)

Conclusion:

The available acute eye irritation data were judged inadequate to meet the endpoint.

Basis for Conclusion:
Two acute eye irritation studies in rabbits were available only as an incomplete data summaries in an HPV submission.

As described in the data summary, Proprietary D (dose not reported) was instilled into the right eye of 6 rabbits. Observations recorded at 1, 24, 48, and 72 hours after treatment reported no positive ocular scores, and found the test material was not irritating to the eyes. The study was conducted according to Good Laboratory Practices (Ref. 6).

An additional study described in the data summary, instilled 0.1 mL of Proprietary D in the right sacs of the right eyes of 6 New Zealand albino rabbits (3/sex). In the 72-hour observation period, redness and chemosis of the conjuctiva were reported. Discharge was also noted in 1 rabbit at 24 hours.

Acute Dermal Irritation (OPPTS Harmonized Guideline 870.2500; OECD Guideline 404)

Conclusion:

The available acute dermal irritation data were judged inadequate to meet the endpoint.

Basis for Conclusion:

An acute dermal irritation study in rabbits was available only as an incomplete data summary in an HPV submission.

As described in the data summary, a single application of 0.5 mL Proprietary D was made to the clipped backs of 6 New Zealand albino rabbits (3/sex) under a gauze patch and wrapped with an air-tight occlusive wrap (duration not reported). The skin of 3 rabbits was abraded. Observations recorded at 24, 48, and 72 hours after treatment reported no irritation on the intact skin, and erythema and edema on the abraded skin. The primary irritation index, according to the method of Draize, was 0.7, and the chemical was not considered to be a primary skin irritant (Ref. 3).

Skin Sensitization (OPPTS Harmonized Guideline 870.2600; OECD Guideline 429)

Conclusion:

The skin sensitization endpoint is not satisfied.

Basis for Conclusion:

No studies were located that followed or were similar to the guideline listed above or otherwise addressed skin sensitization.

SUBCHRONIC TOXICITY

Conclusion:

No available subchronic toxicity data.

Basis for Conclusion:

No pertinent studies were located that addressed the subchronic toxicity endpoints in the guidelines listed below.

Subchronic Oral Toxicity (28-day, 90-day, or combined with reproductive/developmental)

- **Repeated Dose 28-Day Oral Toxicity in Rodents (OPPTS Harmonized Guideline 870.3050; OECD Guideline 407)**

- **90-Day Oral Toxicity in Rodents (OPPTS Harmonized Guideline 870.3100; OECD Guideline 408)**,
- **Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (OPPTS Harmonized Guideline 870.3650; OECD Guideline 422), respectively**.

Subchronic Dermal Toxicity (21/28-day or 90-day).

- **21/28-Day Dermal Toxicity (OPPTS Harmonized Guideline 870.3200 (OECD Guideline 410)**
- **90-Day Dermal Toxicity (OPPTS Harmonized Guideline 870.3250; OECD Guideline 411)**

Subchronic Inhalation Toxicity (90 day)

- **90-Day Inhalation Toxicity (OPPTS Harmonized Guideline 870.3465; OECD Guideline 413)**

REPRODUCTIVE TOXICITY

Conclusion:

No available reproductive toxicity data.

Basis for Conclusion:

No pertinent studies were located that addressed the reproductive toxicity endpoints in the guidelines listed below.

- **Reproduction/Developmental Toxicity Screening (OPPTS Harmonized Guideline 870.3550; OECD Guideline 421)**
- **Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (OPPTS Harmonized Guideline 870.3650; OECD Guideline 422)**
- **Reproduction and Fertility Effects (OPPTS Harmonized Guideline 870.3800; OECD Guideline 416)**

DEVELOPMENTAL TOXICITY

Conclusion:

No available developmental toxicity data.

Basis for Conclusion:

No pertinent studies were located that addressed the developmental toxicity endpoints in the guidelines listed below.

- **Prenatal Developmental Toxicity Study (OPPTS Harmonized Guideline 870.3700; OECD Guideline 414)**
- **Combined Repeated Dose Toxicity Study with the Reproduction/Developmental Toxicity Screening Test (OPPTS Harmonized Guideline 870.3650; OECD Guideline 422)**
- **Reproduction/Developmental Toxicity Screening (OPPTS Harmonized Guideline 870.3550; OECD Guideline 421)**

CHRONIC TOXICITY

Conclusion:

No available chronic toxicity data.

Basis for Conclusion:

No pertinent studies were located that addressed the chronic toxicity endpoints in the guidelines listed below.

- **Chronic Toxicity (OPPTS Harmonized Guideline 870.4100; OECD Guideline 452)**
- **Combined Chronic Toxicity/Carcinogenicity (OPPTS Harmonized Guideline 870.4300; OECD Guideline 453)**

CARCINOGENICITY

Conclusion:

No available carcinogenicity data.

Basis for Conclusion:

No pertinent studies were located that addressed the carcinogenicity endpoints in the guidelines listed below.

- **Carcinogenicity (OPPTS Harmonized Guideline 870.4200; OECD Guideline 451)**
- **Combined Chronic Toxicity/Carcinogenicity (OPPTS Harmonized Guideline 870.4300; OECD Guideline 453)**

NEUROTOXICITY

Conclusion:

No available neurotoxicity data.

Basis for Conclusion:

No pertinent neurotoxicity studies were located that addressed the endpoints in the guidelines listed below.

Delayed Neurotoxicity

- **Acute and 28-Day Delayed Neurotoxicity of Organophosphorus Substances (OPPTS Harmonized Guideline 870.6100; OECD Guideline 418, 419)**
- Note this guideline is not relevant for Proprietary D, which is not an organophosphorus substance.

Neurotoxicity (Adult)

- **Neurotoxicity Screening Battery (OPPTS Harmonized Guideline 870.6200; OECD Guideline 424)**

Developmental Neurotoxicity

- **Developmental Neurotoxicity: Developmental Neurotoxicity Study (OPPTS Harmonized Guideline 870.6300)**

IMMUNOTOXICITY

Conclusion:

No available immunotoxicity data.

Basis for Conclusion:

No pertinent studies of immunotoxicity were located that addressed the endpoints in the guideline listed below.

- **Immunotoxicity (OPPTS Harmonized Guideline 870.7800)**

GENOTOXICITY

Conclusion:

The available gene mutation data were judged inadequate to meet the endpoint.

Basis for Conclusion:

Two *in vitro* gene mutation studies were conducted, but were only available as incomplete robust summaries. Studies of chromosomal aberrations were not available, however, and are needed for adequate characterization of the genotoxicity endpoint.

Gene Mutation *in vitro*

- **Bacterial Reverse Mutation Test (OPPTS Harmonized Guideline 870.5100; OECD Guideline 471)**

An *in vitro* gene mutation study reported negative results in *Salmonella typhimurium* bacteria (strains not specified) and in *Saccharomyces cerevisiae* (D4) at concentrations up to 1.0 µg/plate of Proprietary D, with and without metabolic activation (Ref. 3).

An additional *in vitro* gene mutation study, reported negative results in *Salmonella typhimurium* bacteria (TA 1535, TA 1537, TA 98, and TA 100) at concentrations up to 5,000 µg/plate (which was cytotoxic) of [Formulation 1] (a trade name for Proprietary D), with and without metabolic activation. Negative and positive controls were used (Ref. 4).

No genotoxicity studies relevant to the below categories or to other types of genotoxic effects were located.

Gene Mutation in Vivo
Chromosomal Aberrations in Vitro
Chromosomal Aberrations in Vivo
DNA Damage and Repair

Ecotoxicity

Acute Toxicity to Aquatic Organisms

Conclusion:

The available acute toxicity data for fish, aquatic invertebrates, and algae were judged inadequate to meet the endpoints.

Basis for Conclusion:

A data summary was located for a 96-hour acute toxicity study in bluegill sunfish (*Lepomis macrochirus*) exposed to Proprietary D (Ref. 1). Fish were exposed to aqueous dilutions of the test material at 0, 10, 18, 32, 56, and 100 mg/L. Acetone was used as a carrier solvent. The test waters were completely opaque at the two highest concentrations. The calculated 96-hour LC50 was 12 mg/L (95% CI: 1-18 mg/L). Study details were unavailable to conduct a thorough, independent review of the study. The concentrations in the test waters were not analytically verified; however, the opacity of the water at the two highest concentrations suggest that the test material was not well dissolved. The available data are not adequate to satisfy the acute toxicity endpoint for freshwater fish.

No pertinent acute toxicity studies with marine fish, aquatic invertebrates, or algae were located that followed or were similar to the guideline protocols listed below.

- **Acute Toxicity to Freshwater and Marine Fish (OPPTS Harmonized Guideline 850.1075; OECD Guideline 203)**
- **Acute Toxicity to Freshwater Invertebrates (OPPTS Harmonized Guideline 850.1010; OECD Guideline 202)**
- **Acute Toxicity to Marine/Estuarine Invertebrates (OPPTS Harmonized Guideline 850.1035)**
- **Algal Toxicity (OPPTS Harmonized Guideline 850.5400; OECD Guideline 201)**

Chronic Toxicity to Aquatic Organisms

Conclusion:

No available chronic toxicity data for fish and aquatic invertebrates.

Basis for Conclusion:

No pertinent chronic toxicity studies with fish or aquatic invertebrates were located that followed or were similar to the guideline protocols listed below.

- **Chronic Toxicity to Freshwater and Marine Fish (OPPTS Harmonized Guideline 850.1400; OECD Guideline 210)**
- **Chronic Toxicity to Freshwater Invertebrates (OPPTS Harmonized Guideline 850.1300; OECD Guideline 211)**
- **Chronic Toxicity to Marine/Estuarine Invertebrates (OPPTS Harmonized Guideline 850.1350)**

Acute and Subchronic Toxicity to Terrestrial Organisms

Conclusion:

No available acute and subchronic toxicity data for terrestrial organisms.

Basis for Conclusion:

No pertinent acute oral, dietary, or reproductive toxicity studies with birds and no subchronic toxicity studies with earthworms were located that followed or were similar to the guideline protocols listed below.

- **Acute Oral Toxicity in Birds (OPPTS Harmonized Guideline 850.2100)**
- **Dietary Toxicity in Birds (OPPTS Harmonized Guideline 850.2200; OECD Guideline 205)**
- **Reproductive Toxicity in Birds (OPPTS Harmonized Guideline 850.2300; OECD Guideline 206)**
- **Earthworm Subchronic Toxicity (OPPTS Harmonized Guideline 850.6200; OECD Guideline 207)**

Physical/Chemical Properties

Proprietary D: Reactive brominated flame retardant
CAS
MF
MW
SMILES

Water Solubility (mg/L): No data

Log K_{ow}: No data

Oxidation/Reduction: No data

Melting Point: No data

Vapor Pressure (torr): No data

Odor: No data

Oxidation/Reduction Chemical Incompatibility: No data

Flammability: No data

Explosivity: No data

Corrosion Characteristics: No data

pH: No data

UV/VIS Absorption: No data

Viscosity: No data

Density/Relative Density/Bulk Density: No data

Dissociation Constant in Water: No data

Henry's Law Constant: No data

Environmental Fate

Bioconcentration

Fish: No data

Daphnids: No data

Green Algae: No data

Oysters: No data

Earthworms: No data

Fish Metabolism: No data

Degradation and Transport

Photolysis in the Atmosphere: No data

Photolysis in Water: No data

Photolysis in Soil: No data

Aerobic Biodegradation: No data

Anaerobic Biodegradation: No data

Porous Pot Test: No data

Pyrolysis: No data

Hydrolysis as a Function of pH: No data

Sediment/Water Biodegradation: No data

Soil Biodegradation with Product Identification: No data

Indirect Photolysis in Water: No data

Sediment/Soil Adsorption/Desorption: No data